

Claims

1. A method of inducing undifferentiated cells to differentiate which comprises the step of:

contacting undifferentiated cells with an amount of
5 vpr protein or a functional fragment thereof effective to stimulate differentiation; or

introducing into undifferentiated cells a nucleic acid molecule that comprises a nucleotide sequence that encodes vpr protein or a functional fragment thereof whereby
10 said nucleotide sequence is expressed by said cells.

2. A pharmaceutical composition comprising

a) vpr protein or a functional fragment thereof, or a nucleic acid molecule that comprises a nucleotide sequence that encodes vpr protein or a functional
15 fragment thereof; and

b) pharmaceutically acceptable carrier.

3. A method of treating an individual diagnosed with or suspected of suffering from diseases characterized by hyperproliferating undifferentiated cells which comprises the
20 step of administering to said individual an effective amount of a pharmaceutical composition according to claim 2.

4. A pharmaceutical composition that comprises redifferentiated tumor cells induced to redifferentiate by contacting tumor cells with vpr protein or introducing into
25 tumor cells a nucleic acid molecule that comprises a nucleotide sequence that encodes vpr protein.

5. A method of treating an individual suffering from a disease associated with the loss or disfunction of cells which comprises the step of implanting into said individual
30 a pharmaceutical composition according to claim 4.

6. A method of identifying compounds which inhibit vpr from stimulating differentiation of undifferentiated cells which comprises the steps of

a) contacting, in the presence of a test compound, 5 said undifferentiated cells with an amount of vpr protein sufficient to stimulate differentiation and

b) comparing the differentiation that occurs with the differentiation that occurs when said undifferentiated cells are contacted with vpr protein in the absence of said 10 test compound.

7. A kit for performing the method of identifying compounds which inhibit vpr from stimulating differentiation of undifferentiated cells of claim 6, said kit comprising

a) a first container comprising undifferentiated 15 cells, and

b) a second container comprising vpr protein.

8. A method of identifying compounds that inhibit vpr protein binding to p55, p24, p15, p7 or p6 protein which comprises the steps of:

a) contacting vpr protein or a fragment thereof and 20 p55, p24, p15, p7 or p6 protein or a fragment thereof in the presence of a test compound,

b) determining the level of binding between vpr protein and p55, p24, p15, p7 or p6 protein and

c) comparing that level to the level of binding that 25 occurs when vpr protein or a fragment thereof and p55, p24, p15, p7 or p6 protein or a fragment thereof are contacted in the absence of a test compound.

9. A kit for performing the method of identifying 30 compounds which inhibit vpr protein binding to p55, p24, p15, p7 or p6 protein of claim 8, said kit comprising:

a) a first container comprising vpr protein or a fragment thereof and

b) a second container comprising p55, p24, p15, p7 or p6 protein or a fragment thereof.

10. A method of identifying compounds that inhibit p24 protein binding to p15 or p7 protein which comprises the steps
5 of:

a) contacting p24 protein or a fragment thereof and p15 or p7 protein or a fragment thereof in the presence of a test compound,

b) determining the level of binding between p24
10 protein and p15 or p7 protein and

c) comparing that level to the level of binding that occurs when p24 protein or a fragment thereof and p15 or p7 protein or a fragment thereof are contacted in the absence of a test compound.

15 11. A kit for performing the method of identifying compounds which inhibit p24 protein binding to p15 or p7 protein of claim 10, said kit comprising:

a) a first container comprising p24 protein or a fragment thereof and

20 b) a second container comprising p15 or p7 protein or a fragment thereof.

12. A method of identifying compounds which inhibit p24 aggregation which comprises the steps of:

a) maintaining p24 protein under conditions which
25 promote its aggregation in the presence of a test compound,

b) determining the level of p24 aggregation and

c) comparing that level to the level of aggregation that occurs when p24 protein is maintained under the same conditions in the absence of a test compound.

30 13. A kit for performing the method of identifying compounds which inhibit p24 aggregation of claim 12, said kit comprising

a) a first container comprising p24 protein and

b) a second container comprising p15 protein or MAb 1238.

14. Isolated antibodies which specifically bind to vpr protein produced in eukaryotic cells.

5 15. A method of identifying an individual exposed to HIV
comprising the steps of:

a) contacting a sample with antibodies according to claim 14, and

b) detecting whether said antibodies are bound to

10 vpr.

16. A kit for identifying individuals exposed to HIV comprising

a) a first container comprising antibodies according to claim 14, and

15 b) a second container which contains vpr protein
produced in eukaryotic cells.

17. Isolated vpr protein produced in eukaryotic cells.

18. A method of identifying an individual exposed to HIV comprising the steps of:

20 a) contacting a sample with vpr protein according
to claim 17, and

b) detecting whether said vpr is bound to antibodies.

25 19. A kit for identifying individuals exposed to HIV
comprising

a) a first container comprising vpr protein according to claim 17, and

b) a second container which contains antibodies
30 which specifically bind to vpr protein produced in eukaryotic
cells.

20. A method of enhancing retroviral propagation in cell culture comprising the step of:

adding vpr protein in conjunction with infection of the cells by retrovirus; or

5 introducing into a nucleic acid molecule that comprises a sequence that encodes vpr protein in conjunction with infecting said cells with a retrovirus.

21. A method of identifying compounds that inhibit vpr enhancement of retroviral replication comprising the steps of:

10 a) infecting cells with a retrovirus in the presence of vpr protein and a test compound or infecting with a retrovirus in the presence of vpr protein, cells transformed with a nucleic acid molecule that comprises a nucleotide sequence that encodes vpr, wherein the transformed cells
15 produce vpr protein and

b) comparing the amount of virus produced with the amount of virus produced by infecting cells with a retrovirus in the absence of a test compound.

22. A method of modifying macrophage cells comprising
20 the step of contacting macrophage cells with vpr protein or introducing into the macrophage cells a nucleic acid molecule that comprises a sequence that encodes vpr protein.

23. A method of treating individuals diagnosed with or suspected of suffering from diseases characterized by
25 undesirable activity of macrophage cells comprising the step of administering to such individuals, an effective amount of the pharmaceutical composition of claim 2.

24. Drug delivery particles comprising vpr, p24 and a non-HIV, cell-type specific envelope protein.

30 25. A method of delivering vpr to cells comprising administering a drug delivery particle of claim 24.

26. A fusion compound comprising a biologically active portion linked to a vpr fragment which binds to p24.

27. Drug delivery particles comprising a fusion compound of claim 26, p24 and a cell-type specific envelope protein.

5 28. A nucleic acid molecule that comprises a nucleotide sequence that encodes a fusion compound of claim 26.

29. An expression vector that comprises a nucleic acid molecule of claim 28.

10 30. A host cell that comprises an expression vector of claim 29.

31. A method of delivering a fusion compound to cells comprising administering a drug delivery particle of claim 27 wherein said fusion compounds comprised a biologically active portion linked to a vpr fragment which binds to p24

15 32. A pharmaceutical composition comprising
a) vpr, an immunogenic fragment of vpr or anti-vpr antibodies; and
b) a pharmaceutically acceptable carrier.

20 33. A method of treating an individual exposed to HIV by administering an immunogenic amount of vpr, an immunogenic fragment of vpr or an effective amount of anti-vpr antibodies.